Please amend claim 24 as follows:

24. (AMENDED) The cell surface complex of claim 23, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

A18

Please amend claim 26 as follows:

26. (AMENDED) The method of claim 25, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

A19

IN THE ABSTRACT:

Please amend the Abstract as follows:

(AMENDED) ABSTRACT OF THE DISCLOSURE

A method for modulating an alpha 6 subunit containing integrin-mediated signal transduction is described. The method involves contacting a cell with an effective integrin modulating amount of an alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent. Preferred agents are peptides having the formula f-Met-Leu-X, wherein X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

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**REMARKS**

The amendments have been made to comply with the "Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acids Sequence Disclosures" mailed December 6, 2001, whereby, the sequences in the application are

identified throughout the application. These amendments introduce no new matter and their entry is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification, claims, and Abstract, by the current amendment. The attached page is captioned: "**Version with markings to show changes made.**"

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

DATE: 21 May '02

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the specification:**

IN THE SPECIFICATION:

On page 1, lines 20 - 23, have been amended as follows:

(AMENDED) Synthetic tetrapeptides, particularly f-Met-Ile-Phe-Leu (SEQ ID NO: 1) and f-Met-Leu-Phe-Ile (SEQ ID NO: 2), have also subsequently been shown to evoke neutrophil responses (Rot et al., *Proc. Natl. Acad. Sci. USA* 84:7967-7971, 1987).

On page 2, lines 4 - 11, have been amended as follows:

(AMENDED) In particular, fMet-Leu-Phe-Phe (SEQ ID NO: 3), fMet-Leu-Phe-NHBzl (fMet-Leu-Phe benzylamide), and fNle-Leu-Phe-Tyr (N-formyl-L-norleucyl-Leu-Phe-Tyr) (Kermode et al., *Biochem. J.*, 276: 715-723, 1991) showed both maximal migration (on the order of 20-35 μm) and degranulation (on the order of $ED_{50}$ of $10^{-10}$ to $10^{-11}$). More recent reports suggest that nonformylated peptides may also bind to FPR and can act as potent activators of neutrophil function. For example, Met-Met-Trp-Leu-Leu (SEQ ID NO: 4) is a potent pentapeptide and is comparable in neutrophil function activity to FMLP (Chen et al., *J. Biol. Chem.* 270: 23398-23401, 1995).

On page 10, lines 9 - 15, have been amended as follows:

(AMENDED) Particularly useful peptides are those having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6), most preferably f-Met-Leu-Phe-Phe (SEQ ID NO: 3). Thus, preferred embodiments of the present invention provides a complex of an α6 integrin subunit with a peptide having the formula f-Met-Leu-X where X (SEQ ID NOs: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5),

Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6), most preferably f-Met-Leu-Phe-Phe (SEQ ID NO: 3).

On page 10, lines 17 - 21, have been amended as follows:

(AMENDED) In accord with the present invention, a method for treating an VLA-6 integrin-mediated pathological condition in a mammal comprises administering to the mammal an effective amount of VLA6-IMSTPMA, preferably a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the groups consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 11, lines 8 - 11, have been amended as follows:

(AMENDED) The method comprises administering to a mammal an effective VLA-6 integrin-mediated signal transduction modulating amount of VLA6-IMSTPMA, preferably a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 11, lines 15 - 22, have been amended as follows:

(AMENDED) The method comprises contacting a cell with an effective VLA-6 integrin-mediated signal transduction modulating amount of VLA6-IMSTPMA, preferably a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the groups consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6). Preferably, a method for inhibiting cancer cell metastasis in a mammal comprises administering to the mammal an effective metastasis inhibiting amount of a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the groups consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 11, lines 27 - 31, , have been amended as follows:

(AMENDED) The method comprises administering to the mammal an effective VLA-6 integrin-mediated signal transduction modulating amount of VLA6-IMSTPMA, preferably a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the groups consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 12, lines 15 - 17, have been amended as follows:

(AMENDED) FIG. 1A - FIG. 1B are graphs showing the relationship between the DNA content of normal human peripheral blood mononuclear cells and the amount of fluoresceinated HK-X (f-Met-Leu-Phe-Phe) (SEQ ID NO: 3) binding to the surface of the cells.

On page 13, lines 29 - 30 through to page 14, lines 1-2, , have been amended as follows:

(AMENDED) Preferred VLA6-IMSTPMA agents are certain small peptides having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 24, lines 27 - 29, have been amended as follows:

(AMENDED) The cells were then either exposed to the 100nM FITC-labeled f-Met-Leu-Phe-Phe (SEQ ID NO: 3) (HK-X) or were exposed to a control (vehicle not containing peptide).

IN THE CLAIMS:

Claim 2 has been amended as follows:

2. (AMENDED) The method of claim 1, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6), wherein said peptide is capable binding with an $\alpha_6$ integrin subunit.

Claim 9 has been amended as follows:

9. (AMENDED) The method of claim 1, wherein said peptide is f-Met-Leu-Phe-Phe (SEQ ID NO: 3).

Claim 11 has been amended as follows:

11. (AMENDED) The method of claim 10, wherein said ~~an~~ alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 14 has been amended as follows:

14. (AMENDED) The cell surface complex of claim 13, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO:3) and Phe-Tyr (SEQ ID NO: 6).

Claim 16 has been amended as follows:

16. (AMENDED) The method of claim 15, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 19 has been amended as follows:

19. (AMENDED) The cell surface complex of claim 18, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group

consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 21 has been amended as follows:

21. (AMENDED) The method of claim 20, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 24 has been amended as follows:

24. (AMENDED) The cell surface complex of claim 23, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 26 has been amended as follows:

26. (AMENDED) The method of claim 25, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

IN THE ABSTRACT:

The Abstract has been amended as follows:

(AMENDED) ABSTRACT OF THE DISCLOSURE

A method for modulating an alpha 6 subunit containing integrin-mediated signal transduction is described. The method involves contacting a cell with an effective integrin modulating amount of an alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent. Preferred agents are peptides having the formula f-Met-Leu-X, wherein X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).